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EXAMINER	
HEARD, THOMAS SWEENEY	
ART UNIT	PAPER NUMBER
1654	
MAIL DATE	DELIVERY MODE
12/23/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/645,839	WITTEN ET AL.	
	Examiner	Art Unit	
	THOMAS S. HEARD	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 February 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *42-100* is/are pending in the application.

4a) Of the above claim(s) *43,47,48,50,55-67,70,74,75,77 and 82-100* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *42, 44- 46, 49, 51-54, 68, 69, 71-73, 76, and 78-81* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10/29/2008; 10/07/2008; 04/29/2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of Group I, Claims 42-93, in the reply filed on 2/12/2008 is acknowledged.

Applicants have elected Applicants elect the species of substance P analog, that of [Sar^9, Met $(O_2)l^{11}$]-substance P. Applicants have further elect the route of administration which is inhalation; the amount of substance P which is 5 μM, and the damage to be corrected that is decreased dynamic lung compliance; e.g., a method for increasing dynamic lung compliance.

Applicants have further elect the patent population that is subjects exposed to main stream cigarette smoke. Applicants have stated that the species reads on claims 42, 44- 46, 49, 51-54, 68, 69, 71-73, 76, and 78-81. Claims 43, 47, 48, 50, 55-67, 70, 74, 75, 77, and 82-100 withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected subject matter, there being no allowable generic or linking claim.

Claims 42, 44- 46, 49, 51-54, 68, 69, 71-73, 76, and 78-81 are hereby examined on the merits.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 42, 45-46, 49, 51, 52, 68, 69, 72, 73, 76, 78, and 79 are rejected under 35 U.S.C. 102(b) as being anticipated by Robledo R.F. et al, "NK1-receptor activation prevents hydrocarbon-induced lung injury in mice," Am. J. Physiol. Lung Mol. Physiol (1999), 276:229-238.

The instant invention is drawn to a method of ameliorating or preventing damage caused by cigarette smoke by the administration of a Substance P analog, that of Applicant's elected species of [Sar^9, Met $(O_2)l^{11}$]-substance P. The administration is by inhalation (aerosol) in the concentration ranges of 0.1 µM to 10 µM. The population is that of a subject who has been exposed or will be exposed to main-stream.

Robledo R.F. et al discloses the administration of the Substance P analogue [Sar^9, Met $(O_2)l^{11}$] via aerosol inhalation. The hydrocarbon air mixture was administered to a group of mice who were also administered the Applicant's elected Substance P analogue by inhalation (aerosol) for the treatment regime. Since the mice had not been exposed to side-stream cigarette smoke, the patient population is readable on those who will be exposed because the administration is to a patient who has not had contact with the hydrocarbons of cigarette smoke. Further, the aerosol concentration of the [Sar^9, Met $(O_2)l^{11}$]-substance P was 5 µm readable upon Claims 45 and 46, 51, 52, 68, 69, 71- 73, 78, 79. Claims 49 and 76 drawn to where the substance P analog is administered in an amount sufficient to increase dynamic lung compliance is inherent to the method since the amounts administered are in the ranges disclosed by Robledo and

must provide that function the disclosed amount. Therefore, the invention as claimed is anticipated by the prior art.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 42, 44- 46, 49, 51-54, 68, 69, 71-73, 76, and 78-81 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The instant invention is drawn to analogs of Substance P. Applicants have not provided a limiting definition of what an analog of Substance P is. In fact, the specification envisions that this definition is an ongoing process of discovery. The meaning provided by Applicants is:

These include, but are not limited to: [Met-OH11]-substance P, [Met-OMe11]-substance P, [Nle11]-substance P, [Pro9]-substance P, [Sar9]-substance P, [Tyr8]-substance P, [p-Cl-Phe7,8]-substance P, and [Sar9,Met(02)11]-substance P. The latter analogue is particularly preferred. Bioactive analogs, according to the invention are those which act as competitive inhibitors of SP by binding to the SP receptor (NK-1 receptor). Other derivatives as are known in the art and commercially available (e.g., from Sigma) can be used. In addition, substance P fragments and derivatized substance P fragments may also be used. Substitution, deletion, or insertion of one to eight amino acid residues, and preferably from one to three amino acid residues, **will lead to analogs which can be routinely tested for biological activity**. In addition, functional groups may be modified on SP while retaining the same amino acid backbone. Again, routine testing will determine which of such modifications do not adversely affect biological activity.

Thus, the boundaries for analog is not defined in such a manner as to provide meaning to the word, leaving the term indefinite. Note that analog is a compound that has the same function but not the same structure. Structure is not correlated to function and the connection between the two is indefinite.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 42, 44- 46, 49, 51-54, 68, 71-73, 76, and 78-81 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The MPEP states that the purpose of the written description requirement is to ensure that the inventor had possession, as of the filing date of the application, of the specific subject matter later claimed by him. The courts have stated:

"To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997); In re Gostelli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) ("[T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, no that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d at 1572, 41 USPQ2d at 1966." Regents of the University of California v. Eli Lilly & Co., 43 USPQ2d 1398.

The MPEP lists factors that can be used to determine if sufficient evidence of possession has been furnished in the disclosure of the Application. These include "level of skill and knowledge in the art, partial structure, physical and/or chemical properties, functional characteristics alone or coupled with a known or disclosed correlation between structure and function, and the method of making the claimed invention. Disclosure of any combination of such identifying characteristics that distinguish the claimed invention from other materials and would lead one of skill in the art to the conclusion that the applicant was in possession of the claimed species is sufficient." MPEP § 2163.

Further, for a broad generic claim, the specification must provide adequate written description to identify the genus of the claim. In Regents of the University of California v. Eli Lilly & Co. the court stated:
"A written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." Fiers, 984 F.2d at 1171, 25 USPQ2d at 1606; In re Smythe, 480 F.2d 1376, 1383, 178 USPQ 279, 284985 (CCPA 1973) ("In other cases, particularly but not necessarily, chemical cases, where there is unpredictability in performance of certain species or subcombinations other than those specifically enumerated, one skilled in the art may be found not to have been placed in possession of a genus ...") Regents of the University of California v. Eli Lilly & Co., 43 USPQ2d 1398.

The MPEP further states that if a biomolecule is described only by a functional characteristic, without any disclosed correlation between function and structure of the sequence, it is "not sufficient characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence." MPEP 2163. The MPEP does state that for a generic claim the genus can be adequately described if the disclosure presents a sufficient number of representative species that encompass the genus. MPEP 2163. If the genus has a substantial variance, the disclosure must describe a sufficient variety of species to reflect the variation within that genus. See MPEP 2163. Although the MPEP does not define what constitute a sufficient number of representative species, the courts have indicated what do not constitute a representative number of species to adequately describe a broad generic. In Gostelli, the courts determined that the disclosure of two chemical compounds within a subgenus did not describe that subgenus. In re Gostelli, 872, F.2d at 1012, 10 USPQ2d at 1618.

The factors considered in the Written Description requirement are (1) level of skill and knowledge in the art, (2) partial structure, (3) physical and/or chemical properties,

(4) functional characteristics alone or coupled with a known or disclosed correlation between structure and function, and the (5) method of making the claimed invention.

In the instant case, the claims are drawn to a method of ameliorating or preventing lung damage via the administration of a Substance P analogue.

(1) Level of skill and knowledge in the art:

The level of skill to practice the art of the instantly claimed invention is high with regard to experimental protocols, bioassays and interpretation of the data to a complex model of cellular signaling involved in the Substance P pathway.

(2) Partial structure: (3) Physical and/or chemical properties: and (4) Functional characteristics:

The partial structures are those of Substance P and those that have been modified to contain amino acid substitutions and deletions. Their function is for the Substance P (SP) is a naturally occurring small, molecular weight peptide (11 amino acids) that is localized to the nerves in the airways of several species, including humans. Substance P preferentially activates NK-1 tachykinin receptors.

(5) Method of making the claimed invention:

Chemical synthesis

As stated supra, the MPEP states that written description for a genus can be achieved by a representative number of species within a broad generic. It is unquestionable that Claim 42 and 68 are a broad generic, with respect to all possible

compounds encompassed by the claims. The possible structural variations are limitless to any class of compound described by functional language only.

It must not be forgotten that the MPEP states that if a biomolecule is described only by a functional characteristic, without any disclosed correlation between function and structure of the sequence, it is "not sufficient characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence. "MPEP § 2163.

Here, though the claims may recite some functional characteristics, the claims lack written description because there is no disclosure of a correlation between function and structure of the compounds beyond compounds disclosed in the examples in the specification. There are approximately seven examples and while having written description for those species of Substance P compounds, such as those in Claims 42 and 69, Applicants have not provided sufficient description of what constitutes an Analogue. Applicant's definition of analogue is:

These include, but are not limited to: [Met-OH.sup.11]-substance P, [Met-OMe.sup.11]-substance P, [Nle.sup.11]-substance P, [Pro.sup.9]-substance P, [Sar.sup.9]-substance P, [Tyr.sup.8]-substance P, [p-Cl-Phe.sup.7,8]-substance P, and [Sar.sup.9,Met(0.sub.2).sup.11]-substance P. The latter analogue is particularly preferred. Bioactive analogs, according to the invention are those which act as competitive inhibitors of SP by binding to the SP receptor (NK-1 receptor). Other derivatives as are known in the art and commercially available (e.g., from Sigma) can be used. In addition, substance P fragments and derivatized substance P fragments may also be used. Substitution, deletion, or insertion of one to eight amino acid residues, and preferably from one to three amino acid residues, will lead to analogs which can be routinely tested for biological activity. In addition, functional groups may be modified on SP while retaining the same amino acid backbone. Again, routine testing will determine which of such modifications do not adversely affect biological activity.

There is insufficient description of a common core structure that would allow one of skill in the art to practice the invention as claimed or described in the specification.

Deletion and substitutions break the common core structure and can disrupt the portion of the sequence that confers the functional activity.

The description requirement of the patent statue requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See In re Wilder, 736, F.2d 1516, 1521, 222 USPQ 369, 372-73 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate.")

Accordingly, it is deemed that the specification fails to provide adequate written description for the genus of the claims and does not reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the entire scope of the claimed invention.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 42, 44- 46, 49, 51-54, 68, 69, 71-73, 76, and 78-81 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for attenuating smoke induced cellular damage in the lung, does not reasonably provide enablement for preventing damage caused by cigarette smoke. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The factors to be considered in determining whether a disclosure meets the enablement requirements of 35 U.S.C. 112, first paragraph, have been described in *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir., 1988). The court in Wands states, "Enablement is not precluded by the necessity for some experimentation, such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue', not 'experimentation'" (Wands, 8 USPQ2sd 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations" (Wands, 8 USPQ2d 1404). Among these factors are: (1) the nature of the invention; (2) the breadth of the claims; (3) the state of the prior art; (4) the relative skill of those in the art; (5) the predictability or unpredictability of the art; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

While all of these factors are considered, a sufficient amount for a *prima facie* case is discussed below.

(1) The nature of the invention and (2) the breadth of the claims:

The claims are drawn to a method of ameliorating or preventing damage by cigarette smoke by the administration of Substance P or a substance P analogue. Thus, the claims taken together with the specification imply that the administration of these

compounds would result in the complete absence of cellular damage caused by cigarette smoke.

(3) The state of the prior art:

Robledo R.F. et al, "NK1-receptor activation prevents hydrocarbon-induced lung injury in mice," Am. J. Physiol. Lung Mol. Physiol (1999), 276:229-238 discloses the benefits of Substance P and the Applicant's elected species in reducing the damage of inhaled hydrocarbons from Jet Fuel by the inhalation. Substance P is known to induce NK1-receptor and has shown benefit in its activation by Substance P when the lungs are exposed to environmental toxins, such as cigarette smoke. Substance P analogues are knows in the prior art such as those specifically recited in Claims 42 and 69.

(4) The relative skill of those in the art:

The relative skill of those in the art is high regarding experimental protocols, bioassays and interpretation of the data to a complex model of cellular signaling involved in the Substance P pathway.

(5) The predictability or unpredictability of the art: *(6) The amount of direction or guidance presented and (7) The presence or absence of working examples: and (8) The quantity of experimentation necessary:*

The definition of prevention is provided by AskOxford is "to keep from happening or to stop from doing something. It is impossible to completely prevent damage from occurring in the invention instantly claimed. Cellular damage is so broad that one cannot say the any one component of the cell is free of damage. Since the ability to prevent remains largely unsolved for the Substance P compounds and the analogs

claimed, means for determining and establishing that the method as claimed can prevent is highly unpredictable. The specification has provided a few experimental protocols to infer that Substance P can prevent DNA damage, for example. The the experiment evaluating DNA damage, Applicants have stated that after [t]reatment with SP immediately after SSCS exposure resulted in levels of micronuclei formation comparable to control animals, in both blood and bone marrow cells. That the results were comparable does not mean that damage was not caused to the DNA of the cell even if the damage was benign. The specification does not provide experimental results that would correspond to total absence of damage to the cell, readable on prevention.

Considering the state of the art as discussed by Wands Factors supra and the high unpredictability and the lack of guidance provided in the specification, one of ordinary skill in the art would be burdened with undue experimentation to demonstrate that the administration of Substance P prevents cellular damage. It is the examiner's position that one skilled in the art could not practice the invention commensurate in the scope of the claims without undue experimentation.

Conclusion

No claims are allowed.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Prior art contained in the reference of record can be applied in the next office action.

Applicant should specifically point out the support for any amendments made to the disclosure, including the claims (MPEP 714.02 and 2163.06). Due to the procedure

outlined in MPEP § 2163.06 for interpreting claims, it is noted that other art may be applicable under 35 U.S.C. § 102 or 35 U.S.C. § 103(a) once the aforementioned issue(s) is/are addressed.

Applicant is requested to provide a list of all copending applications that set forth similar subject matter to the present claims. A copy of such copending claims is requested in response to this Office action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Thomas S. Heard whose telephone number is (571) 272-2064. The examiner can normally be reached on 9:00 a.m. to 6:30 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on (571) 272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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